

Lab Highlight—Misra Lab



(left to right: Saurav Misra, Ph.D., Joe Amick, Rick Page, Ph.D., Zhen Xu, Ph.D. and Krystal Newton)

The Misra lab uses structural biology, biophysics and biochemistry to understand two aspects of protein homeostasis: protein quality control (PQC) and protein localization. Our major goal is to understand how the chaperone machinery and the protein degradation machinery interact with each other to carry out PQC in healthy cells, stressed cells and cells in which a defective protein is overexpressed, misprocessed, or dysregulated. Our secondary research direction is to understand the biogenesis and localization of ion channels and transporters.

The component of PQC that we study most intensively is the ubiquitin ligase CHIP. Uniquely among ubiquitin ligases, CHIP binds directly to two crucial ATP-driven chaperones, Hsp70 and Hsp90. CHIP ubiquitinates misfolded proteins (“clients”) that are bound by these chaperones, targeting the defective proteins for degradation. CHIP ubiquitinates a diverse array of clients, including protein kinases, onco- and tumor-suppressor proteins such as p53, and nuclear receptors. CHIP can also ubiquitinate and remove many pathogenic, aggregation-prone proteins such as α -synuclein, tau, huntingtin, Ataxin-3, and SOD1, which cause neurodegenerative disorders such as Parkinson’s, Alzheimer’s, Huntington’s disease, SCA and ALS. Intriguingly, CHIP knockout mice are hypersensitive to stresses and demonstrate symptoms of accelerated aging at the cellular level.

The lab is pursuing a comprehensive characterization of CHIP and its interactions with Hsp70 and Hsp90, with ubiquitin conjugating enzymes, with substrates, and with “co-chaperone” proteins that modulate CHIP-mediated PQC. Dr. Zhen Xu, research associate, identified the basis of CHIP’s dimerization and showed how CHIP recruits specific ubiquitin conjugating enzymes. Her studies are among the first comprehensive studies of ubiquitin conjugating enzyme:ubiquitin ligase interactions, and defined “interaction rules” that are readily applicable to other ligases and ubiquitin conjugating enzymes.

Dr. Rick Page, postdoctoral fellow is characterizing the Hsp70-cochaperone Bag2, which promotes client refolding and inhibits CHIP-mediated ubiquitination. Bag2 was first identified a decade ago as a nucleotide exchange factor (NEF) for Hsp70, but an incorrect structural and mechanism were attributed to it. Dr. Xu solved the structure of the BNB domain of Bag2 and showed how it binds and alters the conformation of Hsp70 to promote nucleotide exchange. Drs. Page validated these structures using NMR and biochemical assays. Furthermore, Dr. Page found that the BNB domain also binds and inhibits the aggregation of misfolded proteins. His results show that oligomers of Bag2 bind to misfolded proteins, and then pass along the misfolded protein to Hsp70 for refolding. He is now characterizing the structural basis for substrate binding by the Bag2-BNB domain.

Dr. Page, Dr. Xu and Joseph Amick, technician, are also determining the structure and mechanism of the N-terminal domain (NTD) of Bag2, which is necessary for the ability of Bag2 to inhibit CHIP. Drs. Page and Xu have determined the structure of the NTD, and have used NMR to show that it inhibits CHIP through an indirect steric mechanism, by interacting with and blocking the ubiquitin conjugating enzymes recruited by CHIP. This is an exciting and novel finding because no similar mechanism of negative regulation of ubiquitination has been found, either for CHIP or for any other ubiquitin ligases. Dr. Page is now structurally characterizing this mechanism. This information will be useful for the design of peptide-based inhibitors for other ubiquitin ligases implicated in cancer or other pathologies.

Drs. Page, Xu and Joe are also studying the biogenesis and membrane localization of the CFTR Chloride channel, which is mutated in patients suffering from Cystic Fibrosis. Together with Dr. Carole Liedtke's group at CWRU, Drs. Page and Xu have characterized the structural basis of the interaction between CFTR and the cytoskeletal adaptor protein filamin, which anchors CFTR to cortical actin and lengthens the residence time of CFTR at the plasma membrane. Joe is mapping the interaction between filamin and RACK1, a β -propeller-type signaling protein that also modulates the localization and the activation of CFTR. The lab's work in this area is intended to identify new mechanisms to increase CFTR Chloride conductance in the airways and epithelial tissues of cystic fibrosis patients, and to reduce Chloride conductance in intestinal epithelia of persons afflicted with bacterially-induced secretory diarrhea.

Department Publications

Ghosh A, Murugesan G, Chen K, Zhang I, Hu Y, Wang Q, **Febbraio M**, Anselmo RM; Marchant K, Barnard J Silverstein RL. CD36 surface expression level on platelets affects functional responses to oxidized LDL and is associated with inheritance of specific genetic polymorphisms. *Blood*, 117:6355-66 (2011).

Chen K, Li W, Major J, Rahaman SO, **Febbraio M**, Silverstein RL. Vav guanine nucleotide exchange factors link hyperlipidemia and a prothrombotic state. *Blood*, 2011, 117:5744-60.

He, J, Lee, JH, **Febbraio M**, Xie, W. The emerging roles of fatty acid translocase. CD36 and the aryl hydrocarbon receptor in fatty liver disease. *Exp Biol Med*, 236:1116-21 (2011).

Nicholls HT, Kowalski G, Kennedy DJ, Risis R, Zaffino LA, Watson N, Kanellakis P, Watt MJ, Bobik A, Bonen A, **Febbraio M**, Lancaster GI, Febbraio MA. Haematopoietic cell restricted deletion of CD36 reduces high fat diet-induced macrophage infiltration and improves insulin signaling in adipose tissue. *Diabetes*, 60:1100-10 (2011).

Sos BC, Harris C, Nordstrom SM, Tran JL, Balázs M, Caplazi P, **Febbraio M**, Applegate MA, Wagner KU, Weiss EJ. Abrogation of growth hormone secretion rescues fatty liver in mice and hepatocyte-specific deletion of JAK2. *J Clin Invest.*, in press. 121:1412-23 (2011).

Rahaman SO, Swat W, **Febbraio M***, Silverstein RL* Vav family Rho guanine nucleotide exchange factors regulate CD36-mediated macrophage foam cell formation. *J Biol Chem*. 286:7010-7 (2011). *co-senior authors.

Kim TW, **Febbraio M**, Robinet P, Dugar B, Greene D, Cerny A, Latz E, Gilmour R, Staschke K, Chisolm G, Fox PL, Dicorleto PE, Smith JD, Li X The Critical Role of IL-1 Receptor-Associated Kinase 4-Mediated NF- κ B Activation in Modified Low-Density Lipoprotein-Induced Inflammatory Gene Expression and Atherosclerosis. *J Immunol.*, 186:2871-80 (2011).

Liu, J., Chen, R., Marathe, G.K., **Febbraio M.**, Zou, W., McIntyre, T.M. Circulating Platelet-activating Factor is Primarily Cleared by Transport, not Intravascular Hydrolysis by Lipoprotein-associated Phospholipase A2 / PAF Acetylhydrolase. *Circulation Research*, 108, 469-77 (2011).

Sung, M., Koonen, D.P.Y.; Soltys, C.; Jacobs, R.L.; **Febbraio M.**; Dyck, J.R.B. Increased CD36 Expression in Middle-Aged Mice Contributes to Obesity-related Cardiac Hypertrophy in the Absence of Cardiac Dysfunction, *Journal of Molecular Medicine*, 89, 459-469 (2011).

Kennedy, D.J., Kuchibhotla, S., Westfall, K.M., Silverstein, R.L., Morton, R.E., **Febbraio, M.** A CD36-Dependent Pathway Enhances Macrophage and Adipose Inflammation and Impairs Insulin Signaling. *Cardiovasc Res.* 89:604-13 (2011).

Wu, C., S. Agrawal, A. Vasanthi, S. Sarkaria, J. Xie, B. M. Liu, Anand-Apte, and **A. Horowitz.** Rab13-dependent trafficking of RhoA is required for directional migration and angiogenesis. *J. Biol. Chem.*, 286: 23511–23520, 2011.

Gong Y, Fan Y, **Hoover-Plow J.** Plasminogen regulates stromal cell-derived factor-1/CXCR4-mediated hematopoietic stem cell mobilization by activation of matrix metalloproteinase-9. *Arterioscler Thromb Vasc Biol.* 2011, Sept;31(9):2035-43.

Sa Q, **Hoover-Plow JL.** EMILIN2 (Elastin microfibril interface located protein), potential modifier of thrombosis. *Throm J.* 2011 May 11;9:9.

H. Unal, R. Jagannathan and **S.S. Karnik** (2011) Mechanism of GPCR-directed Autoantibody in Diseases. The proceedings of the IXth ISCSM (2011) *Advances in Exp Biol. and Med.* (in press)

H. Unal and **S.S. Karnik** (2011) Domain coupling in GPCRs: the engine for induced conformational changes. Trends in *Pharmacol. Sci.* (in press)

Klenotic PA, **Page RC, Misra S,** Silverstein RL. Expression, purification and structural characterization of functionally replete thrombospondin-1 type 1 repeats in a bacterial expression system. *Protein Expr Purif.* 2011 Dec;80(2):253-9. Epub 2011 Jul 29.

Page RC, Clark JG, **Misra S.** Structure of filamin A immunoglobulin-like repeat 10 from Homo sapiens. *Acta Crystallogr Sect F Struct Biol Cryst Commun.* 2011 Aug 1;67(Pt 8):871-6. Epub 2011 Jul 26.

Bulek K, Liu C, Swaidani S, Wang L, Page RC, Gulen MF, Herjan T, Abbadi A, Qian W, Sun D, Lauer M, Hascall V, **Misra S,** Chance MR, Aronica M, Hamilton T, Li X. The inducible kinase IKKi is required for IL-17-dependent signaling associated with neutrophilia and pulmonary inflammation. *Nat Immunol.* 2011 Aug 7;12(9):844-52. doi: 10.1038/ni.2080.

Caini Liu, Shadi Swaidani, Wen Qian, Zizhen Kang, Paige Sun, Yue Han, Chenhui Wang, Muhammet Fatih Gulen, Weiguo Yin, Chunjiang Zhang, Paul L. Fox, Mark Aronica, Thomas A. Hamilton, **Saurav Misra,** Junpeng Deng, and Xiaoxia Li. (2011) "A CC' Loop Decoy Peptide Blocks the Interaction Between Act1 and IL-17RA to Attenuate IL-17- and IL-25-Induced Inflammation." *Science Signaling*, Epub 1 November 2011: ra72.

Doze VA, Papay RS, Collette KM, Gupta MK, Lyons MJ, Davis BA, Luger EJ, Wood SG, Goldenstein BL, Haselton JR, **Perez DM.** Chronic alpha1A-adrenoceptor stimulation improves cognitive function, mood and longevity. *Mol Pharmacol.* 80(4):747-58. 2011.

Perez DM and Doze VA. "Cardiac and Neuroprotection Regulated by alpha1-Adrenergic Receptor Subtypes. *J Recept Signal Transduct Res.* 31(2):98-110, 2011.

Grisanti LA, **Perez DM,** and Porter JE. Modulation of Immune Cell Function by alpha1-Adrenergic Receptor Activation. *Current Topics in Membranes* 67: 113-38, 2011

Das, R., **Plow, E.F.** Phosphatidylserine as an anchor for plasminogen and its plasminogen receptor, Histone 2B, to the macrophage surface. *J Thromb Haem,* 9:339-349, 2011.

Sossey-Alaoui, K., Downs-Kelly, E., Das, M., Izem, L., Tubbs, R., **Plow, E.F.** WAVE3, an actin remodeling protein, is regulated by the metastasis suppressor microRNA, miR-31, during the invasion-metastasis cascade. *Int. J Cancer,* 129:1331-1343, 2011.

Pluskota, E., Dowling, J.J., Gordon, N., Golden, J.A., Szpak, D., West, X.Z., Nestor, C., Ma, Y.Q., Bialkowska, K., Byzova, T., **Plow, E.F.** The integrin co-activator kindlin-2 plays a critical role in angiogenesis in mice and zebrafish. *Blood* 117: 4978-4987, 2011.

Luo, D., Szaba, F.M., Kummer, L.W., **Plow, E.F.,** Mackman, N., Gailani, D., Smiley, S.T. Protective roles for fibrin, tissue factor, plasminogen activator inhibitor-1 and thrombin activatable fibrinolysis inhibitor, but not Factor XI, during defense against the gram-negative bacterium *Yersinia enterocolitica*. 187:1866-1876, 2011.

Augoff, K., Das, M., Bialkowska, K., McCue, B., **Plow, E.F.,** Sossey-Alaoui, K. miR-31 is a broad regulator of [beta]1-integrin expression and function in cancer cells. *Mol Cancer Res.* In Press, 2011.

Wolf, D., Hohmann, J.D., Wiedmann, A., Bledzka, K., Blankenbach, H., Marchini, T., Gutte, K., Zeschky, K., Bassler, N., **Plow, E.F.,** et al. Binding of CD40L to Mac-1's domain involves the EQLKKSRTL motif and mediates leukocyte recruitment and atherosclerosis-but does not affect immunity and thrombosis in mice. *Circ Res.* In press 2011

Neelakantan T. Vasudevan, Maradumane L. Mohan, Manveen K. Gupta, Afshan K. Hussain, and **Sathyamangla V. Naga Prasad**. Inhibition of protein phosphatase 2A activity by PI3K γ regulates β -adrenergic receptor function. *Molecular Cell* 41, 636–648, March 18, 2011.

Abu Jawdeh BG, Khan S, Deschenes I, Hoshi M, Goel M, Lock JT, Shinlapawittayatorn K, Babcock, G., Lakhe-Reddy S, Decaro G, Yadav SP, Mohan ML, **Naga Prasad SV**, Schilling WP, Ficker E, Schelling JR. Phosphoinositide Binding Differentially Regulates NHE1 Na⁺/H⁺ Exchanger-Dependent Proximal Tubule Cell Survival. *J Biol Chem* 2011 Oct. 21 [Epub ahead of print].

Neelakantan T. Vasudevan, Maradumane L. Mohan, Shyamal K. Goswami and **Sathyamangla V. Naga Prasad**. Regulation of beta –adrenergic receptor function- an emphasis on receptor resensitization. *Cell Cycle*, Volume 10, Issue 21, November 1, 2011. (Review article)

Manveen K. Gupta, Zhong-Hui Duan, Sadashiva S. Karnik and **Sathyamangla V. Naga Prasad**. MicroRNAs Telltale Effects on Signaling Networks in Cardiomyopathy. (Book Chapter, Cardiomyopathies- From Basic Research to Clinical Management).

Hong Qu, Yizeng Tu, Xiaohua Shi, Hannu Lajava, Moin A. Saleem, Sanford J. Shattil, **Koichi Fukuda**, **Jun Qin**, Matthias Kretzler and Chuyanyue Wu. Kindlin-2 regulates podocyte adhesion and fibronectin matrix deposition through interactions with phosphoinositides and integrins. *J. Cell Sci.* 2011;124, 879-891.

Koichi Fukuda, James D.R. Knight, Grzegorz Piszcaek, Rashmi Kothary and **Jun Qin**. Biochemical, proteomic, structural, and thermodynamic characterizations of ILK: cross-validation of the pseudokinase. *J. Biol. Chem.* 2011 (in press)

R. C. Wirka, S. Gore, **D. R. Van Wagener**, D. E. Arking, S. A. Lubitz, K. L. Lunetta, E. J. Benjamin, A. Alonso, P. T. Ellinor, J. Barnard, M. K. Chung, and J. D. Smith. A Common Connexin-40 Gene Promoter Variant Affects Connexin-40 Expression in Human Atria and Is Associated with Atrial Fibrillation. *Circ. Arrhythm. Electrophysiol.* 4 (1):87-93, 2011.

Van Wagener, D.R. Chronic vagal nerve stimulation for the treatment of human heart failure: progress in translating a vision into reality. *European Heart J.* 32:788-790, 2011.

F. Mayyas, S. Sakurai, R. Ram, J. Rennison, E. S. Hwang, L. Castel, B. Lovano, M. L. Brennan, D. Bibus, B. Lands, J. Barnard, M. K. Chung, and **D. R. Van Wagener**. Dietary ω 3 fatty acids modulate the substrate for post-operative atrial fibrillation in a canine cardiac surgery model. *Cardiovasc Res.* 89:852-861, 2011.

S. Nattel and **D. R. Van Wagener**. Atrial fibrillation: Therapy with omega-3 fatty acids-is the case closed? *Nat.Rev.Cardiol.* 8 (3):126-128, 2011.

N. A. Estes, III, R. L. Sacco, S. M. Al-Khatib, P. T. Ellinor, J. Bezanson, A. Alonso, C., Antzelevitch, R. G. Brockman, P. S. Chen, S. S. Chugh, A. B. Curtis, J. P. DiMarco, K. A. Ellenbogen, A. E. Epstein, M. D. Ezekowitz, P. Fayad, B. F. Gage, A. S. Go, M. A. Hlatky, E. M. Hylek, M. Jerosch-Herold, M. A. Konstam, R. Lee, D. L. Packer, S. S. Po, E. N. Prystowsky, S. Redline, Y. Rosenberg, **D. R. Van Wagener**, K. A. Wood, L. Yue, and E. J. Benjamin. American Heart Association Atrial Fibrillation Research Summit: A Conference Report From the American Heart Association. *Circ.* (124):363-372, 2011.

Y. H. Cheng, W. Li, T. A. McElfresh, X. Chen, J. M. Berthiaume, L. Castel, X. Yu, **D. R. Van Wagener**, and M. P. Chandler. Changes in myofilament proteins, but not calcium regulation, are associated with a high fat diet-induced improvement in contractile function in heart failure. *Am J Physiol Heart Circ.Physiol* 301 (4):H1438-H1446, 2011.

F. Rader, **D. R. Van Wagener**, P. T. Ellinor, A. M. Gillinov, M. K. Chung, O. Costantini, and E. H. Blackstone. Influence of Race on Atrial Fibrillation after Cardiac Surgery. Report From the American Heart Association. *Circ.* (124):363-372, 2011.

Shen, J and **Wu Q**. Corin: a protease. *Kidney International* 2011;79:138-139.

Antalis TM, Bugge T, **Wu Q**: Membrane-anchored serine proteases in health and disease. *Prog. Mol. Biol. Transl. Sci.* 2011;99:1-50.

Chou H, Hsieh C, Yang H, Wang L, Arakawa Y, Brown K, **Wu Q**, Lin F, Peters M, Fung JJ, Lu L, Qian S: Hepatic stellate cells regulate immune response via induction of myeloid suppressor cells. *Hepatology* 2011;53:1007-19.

Wu Q, Jiang W: Teamwork: industry and academic perspective. *ASBMB Today* March 2011;26-27.

Jiang J, Wu S, Wang W, Chen S, Peng J, Zhang X, **Wu Q**: Ectodomain shedding and autocleavage of the cardiac membrane protease corin. *J. Biol. Chem.* 2011;286:10066-72.

Qi X, Jiang J, Zhu M, **Wu Q**: Human corin isoforms with different cytoplasmic tails that alter cell surface targeting. *J Biol Chem* 2011;286:20963-20969.

Peng J, Jiang J, Wang W, Qi X, Sun XL, **Wu Q**: Glycosylation and processing of pro-B-type natriuretic peptide in cardiomyocytes. *Biochem Biophys Res Commun* 2011;411:593-598.

Xu-Cai YO, Shen J, Chen S, Zhou Y, LaRusch GA, Stavrou E, Schnaier A, **Wu Q**: Factor XII gene mutation in the Hageman family. *J Thromb Haemost* 2011;9:2329-31.

Dong N, Chen S, Wang W, Zhou Y, **Wu Q**: Corin in clinical laboratory diagnostics. *Clin Chim Acta* (in press)

Qu, H., Tu, Y., Shi, X., Larjava, H., Saleem, M.A., Shattil, S.J., Fukuda, K., **Qin, J.**, Kretzler, M., and Wu, C. Kindlin-2 regulates podocyte adhesion and fibronectin matrix deposition through interactions with phosphoinositides and integrins. *J. Cell. Sci.* 124:879-91, 2011

Sopko, N., Qin, Y.L., Finan, A., Dadabayev, A., Chigurupati, **Qin, J.**, S., Penn, M., and Gupta, S. Significance of thymosin b4 and implication of PINCH-1-ILK-a-parvin complex in human dilated cardiomyopathy. *PLoS One*, 6:e20184, 2011.

Ithychanda, S.S. and **Qin, J.** Evidence for multisite ligand binding and stretching of filamin by integrin and migfilin. *Biochemistry*, 50:4229-31, 2011.

Fukuda, K., Knight, J.D.R., Piszczek, G., Kothary, R., and **Qin, J.** Biochemical, proteomic, structural, and thermodynamic characterizations of ILK: Cross-validation of the pseudokinase. *J. Biol. Chem.*, 286:21886-95, 2011.

Perera, H.D., Ma, Y.Q., Yang, J., Hirbawi, J. **Plow, E.F.**, and **Qin, J.** Membrane targeting of the N-terminal ubiquitin-like domain of kindlin-2 is crucial for its regulation of integrin activation. *Structure*, in press, 2011.

Das, M., Ithychanda, S., **Qin, J.**, and **Plow, E.F.** Filamin and migfilin as regulators of integrin activation in endothelial cells and neutrophils. *Plos One*, 6:e26355, 2011.

Liu, J.M., Fukuda, K., Xu, Z., Ma, Y.Q., Hirbawi, J., Wu, C., **Plow, E.F.**, and **Qin, J.** Structural basis for the phosphoinositide binding of kindlin-2 PH domain in regulation of integrin activation, *J. Biol. Chem.*, in press, 2011.

Vinogradova, O. and **Qin, J.** NMR as a Unique Tool in Assessment and Complex Determination of Weak Protein-Protein Interactions. *Top. Curr. Chem.*, in press, 2011.

Altuntas CZ, Daneshgari F, Sakalar C, Goksoy E, Gulen MF, Kayran M, **Qin J**, Li, X, Touhy VK. Autoimmunity to Uroplakin II Causes Cystitis in Mice: A Novel Model of Interstitial Cystitis. *European Urol.*, in press, 2011.

Caini Liu, Shadi Swaidani, Wen Qian, Zizhen Kang, Paige Sun, Yue Han, Chenhui Wang, Muhammet Fatih Gulen, Weiguo Yin, Chunjiang Zhang, Paul L. Fox, Mark Aronica, Thomas A. Hamilton, **Saurav Misra**, Junpeng Deng, and Xiaoxia Li. (2011) "A CC' Loop Decoy Peptide Blocks the Interaction Between Act1 and IL-17RA to Attenuate IL-17- and IL-25-Induced Inflammation." *Science Signaling*, Epub 1 November 2011: ra72.

Deshmukh L, Meller N, Alder N, **Byzova T**, Vinogradova O. Tyrosine phosphorylation as a conformational switch: A case study of integrin Beta3 cytoplasmic tail. *J Biol Chem*. 2011 Sep 28 [Epub ahead of print].

Somanath PR, **Podrez EA**, Chen J, Ma Y, Marchant K, Antoch M, **Byzova TV**. Deficiency in core circadian protein Bmal1 is associate with a prothrombotic and vascular pheonotype. *J Cell Physiol*. 2011 Jan;226(1):132-40.

Malinin NL, West XZ, **Byzova TV**. Oxidation as "the stress of life". *Aging* (Albany NY). 2011 Sep;3(9):906-10.

Goc A, Choudhary M, **Byzova TV**, Somanath PR. TGFβ- and bleomycin-induced extracellular matrix synthesis is mediated through Akt and mammalian target of rapamycin (mTOR). *J Cell Physiol*. 2011 Nov;226(1):3004-13.

McCabe NP, Kerr BA, Madajka M, Vasanji A, **Byzova TV**. Augmented osteolysis in SPARC-deficient mice with bone-residing prostate cancer. *Neoplasia* 2011 Jan;13(1):31-9.

Feng, W, Madajka M, Kerr, BA, Mahabeleshwar GH, Whiteheart SW, **Byzova TV**. A novel role for platelet secretion in angiogenesis: mediating bone marrow-derived cell mobilization and homing. *Blood*. 2011 Apr 7;117(14):3893-902. Epub 2011 Jan 11. Erratum in: *Blood*. 2011 Jun 30;117(26):7187.

Invited Lectures

Tatiana Byzova, Ph.D.

Invited Speaker: "Tumor interactions with local and systemic environments", University of California, San Diego Seminar Series, January 24-25, 2011.

Invited Speaker: Harvard University Seminar Series, Boston, MA, February 15, 2011.

Invited Speaker: "Integrin signaling in vascular function", Gordon Research Conference on Vascular Cell Biology, Ventura, CA, February 20-25, 2011.

Keynote Speaker: "A novel molecular link between oxidative stress, inflammation and vascularization", The Nora Eccles Harrison Cardiovascular Research and Training Institute, Cardiovascular Symposium, Molecular Medicine Program, University of Utah, Salt Lake City, UT, March 17, 2011.

Keynote Speaker: "Integrins in angiogenesis and inflammation", Fondazione Piemontese per la Ricerca sul Cancro, Institute of Cancer Research and Treatment, Turino, Italy, May 26-29, 2011.

Invited Speaker: "Toll-like receptors and their endogenous ligands in inflammation and angiogenesis", Gordon Research Conference on Angiogenesis, Salve Regina University, Newport, RI, August 21-25, 2011

Invited Speaker & Session Chair: "Regulations of angiogenesis by innate immunity and oxidative damage", 6th Annual Frontiers of Clinical Investigation Symposium, Vascular Disease 2011: Bench to Bedside, October 13-14, 2011

Invited Speaker: "Integrin-kindlin axis in angiogenesis and inflammation", NAVBO Biology of Signaling in the Cardiovascular System Workshop II, Hyannis, MA, October 19, 2011.

Invited Speaker: "Kindlins in blood cell responses", American Heart Association Scientific Sessions 2011, Orange County Convention Center, Orlando, FL, November 12-16, 2011.

Maria Febbraio, Ph.D.

Invited Speaker: University of Connecticut Health Center, Center of Vascular Biology, Farmington, CT, September 6, 2011.

Jane Hoover-Plow, Ph.D.

Invited Speaker: "Maximizing stem cell therapy", International Symposium on Frontiers in Cardiovascular Diseases, Wuhan, China, April 2-7, 2011.

Edward F. Plow, Ph.D.

Invited Speaker: "Integrin activation mechanisms", International Symposium on Frontiers in Cardiovascular Diseases, Wuhan, China, April 2-7, 2011.

Invited Speaker: Gordon Research Conference on Fibronectin & Integrins, Lucca/Pisa, Italy, May 1-6, 2011.

"Plasminogen activation on macrophages", International Society of Thrombosis & Hematosis (ISTH) meeting, Kyoto, Japan, July 23-28, 2011.

ATVB chairman & moderator of plenary session, ATVB conference, Chicago, IL, April 28-30, 2011.

Session Moderator on Lipid Metabolism & Lecture: "Integrin activation in angiogenesis & vascular biology", AHA Scientific Sessions 2011, November 12-16, 2011.

Sathyamangla N.V. Prasad, Ph.D.

Invited Speaker: Jawaharal Nehru University, New Delhi, India, April 14, 2011.

Jun Qin, Ph.D.

Invited Speaker: "Molecular elucidation of integrin signaling and its dysregulation", Scripps Research Institute, January 7, 2011.

Invited Speaker: FN, Integrins and Related Molecules Gordon Conference, Il Ciocco Hotel & Resort, Lucca (Barga), Italy, May 1-6, 2011.

Qing Wang, Ph.D.

Invited Speaker: Computing in Cardiology 2011, Hangzhou, China, September 18-21, 2011.

Invited Speaker: 2nd International Symposium on Diabetes, Obesity and Cardiovascular Disease, University of Hong Kong, Hong Kong, China, September 23-25, 2011.

"Advances in Molecular Genetics and Translational Research of Coronary Artery Disease", 22nd Great Wall International Congress of Cardiology & Asia Pacific Heart Congress 2011, Beijing, China, October 13-16, 2011.

Qingyu Wu, M.D., Ph.D.

"New molecular insights into hypertension and heart disease", Shanghai Expo Symposium on Medical Sciences and Public Health, Shanghai, China, September 21-22, 2010.

Invited Speaker: Danish National Research Foundation, Copenhagen, Denmark, September 22-24, 2011.

"The membrane serine protease corin: discovery and function studies", Chao Tian-Qin International Symposium on Protein Research, Xiamen, China, December 5-8, 2010.

"Type II transmembrane serine proteases in cardiovascular disease and cancer", Center for Proteases and Cancer, Aarhus University, Denmark. September 23-24, 2011.

"The protease corin in hypertensive disease", Department of Cell Biology, University of Alabama at Birmingham, Birmingham, AL, November 9, 2011

Abstracts & Oral Presentations

Abstract: **Koichi Fukuda**, James D.R. Knight, Grzegorz Piszczek, Rashmi Kothary and Jun Qin.

"Cross-validated analysis of ILK: Conclusive evidence for the pseudokinas." 2011 Gordon Research Conference on Fibronectin, Integrins & Related Molecules. Il Ciocco Hotel and Resort, Lucca (Barga), Italy, May 1-6, 2011; **Jane Hoover-Plow, Ph.D.**, ATVB conference, Chicago, IL, March 14, 2011.

Oral Presentation: **Riku Das, Ph.D.**, "Plasminogen as a Modulator of Macrophage Foam Cell Formation", Spring ATVB 2011 Meeting, Chicago, IL, April 28-30, 2011; **Qiuyun Chen, Ph.D.**, "Therapeutic potential of MOG1", AHA Scientific Session 2011, November 11-16, 2011; **Arie Horowitz, D.Sc.**, "Co-trafficking of Syrx and RhoA integrates junction disassembly and cell migration in response to VEGF", Gordon Research Conference, Ventura, CA, February 20-23, 2011; **Elzbieta Pluskota, Ph.D.**, "Kindlin-2 is a novel regulator of hemostasis", AHA Scientific Sessions, Orlando, FL, November 12-16, 2011.

Grants

Qingyu Wu, PI: R01 (NIH/NICHHD) for the period 2/1/11—1/31/16 (\$1.67M), project entitled, “Serine protease corin in pregnancy-induced hypertension”.

Qing Wang, PI: AHA Clinical Investigator Award for the period 1/1/11—12/31/12 (\$150,000), project entitled, “Cellular and molecular mechanisms for chromosome 9p21-linked coronary artery disease”.

Gong-Qing Shen, PI: AHA SDG for the period 1/1/11—12/31/14 (\$308,000), project entitled, “Identification of Novel Candidate Genetic Determinants of CAD Risk Factors on chromosome 15q25”.

Jun Qin, PI: R01 (NIH/NIGMS) renewal for the period 7/5/11-6/30/15 (\$1,226,460), project entitled, “Molecular Elucidation of Integrin Signaling”.

Sadashiva Karnik, PI: R21 (NIH/NHLBI) for the period 8/1/11-5/31/13 (\$471,000), project entitled, “AT1R-regulated nuclear functions of Gb2”.

Riku Das, PI: AHA SDG for the period 7/1/11-6/2015 (\$308,000), project entitled, “Plasminogen as a modulator of macrophage foam cell formation during atherosclerosis”; ATVB 2011 Travel Award for Young Investigators for her oral presentation at the 2011 ATVB meeting in Chicago.

David Van Wagoner, PI: NIH (Subcontract with CWRU) for the period 8/15/2010-4/30/14 (\$140,152) project entitled, “Phenotypic Characterization of nitric oxide regulation of cardiac function by MRI”.

Khalid Sossey-Alaoui, PI: Pilot Grant (CCCC) for the period 11/1/11-10/31/12 (\$33,591), project entitled, “Developing Novel miR-based Chemotherapeutics and Diagnostic Platforms for Triple-negative Breast Cancers”.

Edward F. Plow, PI: NIH (NHLBI) renewal for the period 7/1/11—6/30/2016 (\$392,500), project entitled “Classical and Alternative Pathways of Fibrinolysis”.

Awards

Tatiana Byzova, Ph.D., Investigator Recognition Award (Biannual Award for Contribution to Hemostasis), International Society on Thrombosis and Hemostasis (ISTH) meeting, Kyoto, Japan, July 22-29, 2011.

Neelakantan T. Vasudevan, Ph.D., Irvine H. Page Award for best publication (2010-2011), Molecular Cardiology Fellow Seminar Series

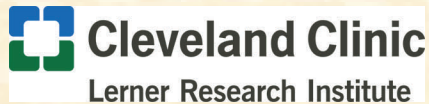
Richard Page, Ph.D., Bernadine Healy Award for best presentation (2010-2011), Molecular Cardiology Fellows Seminar Series

Bethany Kerr, Ph.D.: NIH Ruth L. Kirstein National Service Award (NCI); Hot Topic Lecturer at Cell Biology of Megakaryocytes and Platelets Gordon Research Conference; International Society on Thrombosis and Haemostasis New Investigator Travel Award; Baxter Healthcare Corporation Young Investigator Award; Lerner Research Institute Retreat Best Poster

Xiaoxia Z. West: First place graduate poster at the 5th Cleveland State Interdisciplinary Research Conference; Excellence in Angiogenesis and Vascular Biology Award, Angiogenesis Research Center, Cleveland Clinic; Bumpus Award, semi-finalist, Cleveland Clinic.

Lerner Research Institute
Department of Molecular Cardiology
9500 Euclid Avenue / NB50
Cleveland, OH 44195

Phone: 216-445-0422
Fax: 216-445-8204
E-mail: destefs@ccf.org



We're on the Web:
[www.lerner.ccf.org/
molecard/](http://www.lerner.ccf.org/molecard/)

Department News

Introducing Molecular Cardiology's newest members....



Daniel
Born: March 13, 2011
Menggui Huang
(Hoover-Plow lab)



Katherine Hope
Born: March 25, 2011
Julie Rennison, Ph.D.
(Van Wagoner Lab)

Fond Farewell.....

Dr. Ted Magalev retired on July 31, 2011. We wish to thank him for his years of service and wish him well.

After 40+ years of service, Dr. Subha Sen retired on July 31, 2011. Our best wishes to her for a happy retirement!



Tim Burke (Plow Lab) moved to Colorado in July. Tim will be getting married sometime next year. Good luck and best wishes!!



Zack
Born: April 27, 2011
Yanqing Gong, Ph.D.
(Hoover-Plow Lab)



Samira Suha
Born: April 27, 2011
Rajani Tendulkar
(Administrator)